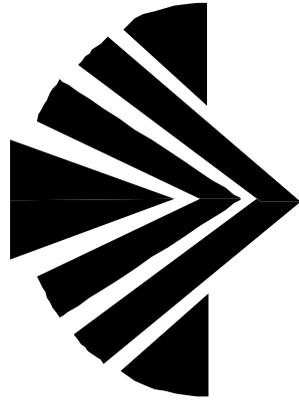




The Fibroid Study staff: (front row) Glenn Heartwell, Lynda Tatum, Deborah Cousins
(back row) Berrit Stroehla, Susie Covington, Donna Baird

National Institute of Environmental Health Sciences / National Institutes of Health / Department of Health and Human Services



UTERINE FIBROID STUDY

NEWS

December 2003

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UTERINE FIBROID STUDY
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WHAT'S GOING ON WITH THE UTERINE FIBROID STUDY?

We are glad to report that so many of you helped us reach our goal of interviewing at least 80% of follow-up participants in 2002. We tried to talk with all the women who were premenopausal at the time of our first interview in 1996-1999.

Here are some statistics from that follow-up that may be of interest to you:

Out of the 1229 Follow-up Participants:

- 344 (28%) reported having at least 1 sonogram since the first telephone interview
- 12 (1%) reported having a myomectomy since the first telephone interview
- 8 (0.7%) reported having a hysteroscopic resection since the first telephone interview
- 46 (4%) reported having an MRI of the pelvic area.
- 66 (5%) reported having a hysterectomy
- 3 (0.2%) reported having a Uterine Artery Embolization

We're getting ready for another Follow-up cycle which we're planning to begin in March, 2004. This will be our last Follow-up interview. Please participate if you are able! Your experiences matter!

We want to hear from you:

- If you have moved since we spoke with you last or have a new phone number at home or at work, please call us. We've added a toll-free number: 1-800-948-7552, extension 365. If you get a voice mail, please leave your new contact information and we'll be sure to update your information.
- If you want to ask us any questions about the study, tell us something about yourself or suggest ideas or questions for future studies don't hesitate to call. Please leave us your phone number and we'll return your call as soon as we can!

Finding Genes for Fibroids

The Finding Genes for Fibroids study, is a family study being conducted by the Center for Uterine Fibroids, Brigham and Women's Hospital in Boston. The study aims to identify genetic factors that increase susceptibility to fibroids. A family is eligible to participate if two full sisters in the family have (or have had) fibroids. Many sister pairs in the family can participate by completing a questionnaire and giving a blood sample. Families from all over the world can participate since the blood sample is mailed to the clinic. For more information, visit this study's Web site: <http://www.fibroids.net/html/study1.htm>

Web Resources

Women's Health Information

www.womenshealthnetwork.org National Women's Health Network
www.4woman.gov National Women's Health Information Center

Menopause Information

www.menopause.org North American Menopause Society
www.menopause.org.au Australian Menopause Society

Fibroid Information

www.fibroids.net Center for Uterine Fibroids, Brigham and Women's Hospital, Boston
www.fda.gov/fdac/features/2001/601_tech.html Food and Drug Administration
www.nuff.org National Uterine Fibroids Foundation

KEEP IN TOUCH WITH US

We want to keep all participants informed about the findings from the Uterine Fibroids Study, but we need your help. If you have moved or changed your telephone number, please call us at our toll-free number, 1-800-948-7552 extension 365, and give us your new contact information.



More Studies on Fibroids in Progress:

Fibroid Growth Study

Little is known about the rate of growth for fibroids. This study, funded by the National Institutes of Health (NIH), is currently being conducted by researchers at the University of North Carolina Hospitals. The Fibroid Growth Study will address the following questions:

- Do fibroids from the same woman grow together or do some grow rapidly while others remain stable or shrink?
- How variable is fibroid growth between women?
- Is growth continuous over time or are there growth spurts?

In this study, fibroids are measured with magnetic resonance imaging (MRI) at entry, after 3 months, 6 months, and a year. Participants who decide with their doctors to have a hysterectomy or myomectomy during the study are asked to donate uterine tissue. Goals of the study include:

- Describing fibroid growth over time, and
- identifying biological differences between growing and nongrowing fibroid tissue.

If factors that cause fibroid growth can be identified, this knowledge can be used to develop treatments to prevent fibroid growth. For more information, you can visit this study's Website: <http://www.niehs.nih.gov/fibroids/home.htm>

Experimental Trial of CDB-2914, a Progesterone Receptor Antagonist

The purpose of this NIH study is to compare fibroid size, symptoms, and hormone levels in treated and untreated women. Women with fibroids who are planning to have a hysterectomy for fibroids, but are willing to participate in the trial for 4 menstrual cycles before having the surgery, are currently being enrolled.

After a baseline menstrual cycle participants take either CDB-2914 or a placebo for the next three menstrual cycles and effects of the treatment will be measured. If CDB-2914 appears to have no adverse effects, but reduces fibroids size and symptoms it will continue to be evaluated as a possible noninvasive fibroid treatment.

For more information, visit this study's Web site:
http://clinicalstudies.info.nih.gov/detail/A_2002-CH-0287.html

NEW FINDINGS FROM THE UTERINE FIBROID STUDY

What Has The Fibroid Study Learned about Risk Factors for Uterine Fibroids?

Your information has helped us to understand more about these risk factors:

- body weight
- exercise
- age of menarche
- prenatal DES exposure

Thank you for your patience while the data from this study was being prepared and analyzed. Dr. Baird is preparing to publish these results in the near future, but wants you to be the first to know the preliminary results!

We know that many of you look forward to receiving more results after participating in such a worthwhile study for so many years, and we look forward to continuing to send you results as we complete more data analysis. You can also check the National Institute of Environmental Health Sciences web site located at: http://dir.niehs.nih.gov/direb/fibroids/home_fib.htm.

Weight

Physicians who treat fibroids have noted that women who are overweight or obese appear to be more likely to have fibroids. In our study the risk of fibroids among women who were overweight was small – that is, being overweight increases your risk of fibroids only about 10%-20%. We used the Centers for Disease Control's (CDC) definition for overweight and obese. These definitions are based on BMI (body mass index), which is a measure of weight and height. A BMI of 25-29 is considered overweight and a BMI of 30 or more is considered obese. Calculate your BMI on the CDC website: www.cdc.gov/nccdphp/dnpa/bmi/calc-bmi.htm or use the following formula based on your height in inches and your weight in pounds:
 $(\text{weight} \times .4545) / (\text{height} \times .0254)^2$

Exercise

You may remember all those questions we asked you about how many hours you spent walking, or in moderate and vigorous exercise. While walking and moderate exercise does not appear to change your risk of fibroids, we found vigorous exercise of 3 or more hours per week reduces your risk of fibroids by about 30-40%! There is one report in the literature showing a reduced risk for women who were athletes in their youth, but we are not aware of any other studies that have shown a relationship between exercise and fibroids. By the way, if you walk or participate in moderate exercise, please keep it up! Exercise, even low intensity exercise, is an important way to maintain a healthy heart and weight.

Age of Menarche

Menarche means 'first menstrual period'. Women who begin to have periods at an early age seem to be at higher risk for fibroids than women whose periods begin late. For each year women started periods before the age of 14, we found a nearly 25% increase in the risk of fibroids. That means a woman who started having periods at age 12 would be around 50% more likely to develop fibroids than a woman whose periods started at age 14. This has also been reported in other studies of fibroids for both black and white women.

Prenatal DES Exposure

Exposure to hormones before birth may influence the adult uterus. Laboratory animals show increased risk of uterine fibroids when they have early exposure to the estrogen, diethylstilbestrol (DES). You may remember that we asked you if you had been exposed to DES before you were born. Some of your mothers were given the drug while they were pregnant because it was thought to prevent miscarriage, although subsequent studies have shown that it wasn't effective. All five of the black women who reported DES exposure had fibroids. About 20 white women reported that their mothers had taken DES while pregnant, and these women were about twice as likely to have fibroids as those who reported that their mothers were not taking DES. Furthermore, DES-exposed women tended to have larger fibroids. The number of pregnant women who took DES is small, so DES can't account for the common finding of fibroids in the general population. However, this finding suggests that early life exposures can affect fibroid development. Further laboratory research may help identify the changes that occur in the developing uterus that will result in fibroid development later in life.

New Treatments for Fibroids:

The traditional treatments for fibroids are symptom management (pain medication and/or medication to reduce bleeding) and surgery. A surgeon may remove the fibroids (myomectomy) while leaving the uterus, or she/he may remove the whole uterus (hysterectomy). Newer treatments include endometrial ablation, myolysis, and uterine artery embolization. *All these treatments have side effects and risks. Discuss and consider the pros and cons of any treatment with your health provider before making a decision about your health.* Treatments that have shown promise in small research studies are low-dose mifepristone (pill) and thermoablative ultrasound guided by magnetic resonance imaging.

These newer treatments are described briefly below.

Endometrial Ablation

This minimally invasive procedure is used to alleviate abnormal uterine bleeding. It destroys the lining of the uterus. It was first done with lasers, now can be done with heat (hot water, electrical energy) or freezing.

Myolysis

This minimally invasive procedure destroys the blood vessels of each treated fibroid, thus cutting off the blood supply to the tumor tissue. It can be done with heat using lasers or electrical current, or it can be done with cold using liquid nitrogen.

Uterine Artery Embolization

This minimally invasive procedure is designed to cut off blood to fibroids so they die. A small tube is threaded from the groin into the uterine artery and small particles are injected through the tube to block the arteries. A clot forms around the particles and the blood flow to the fibroids is blocked.

Thermoablative Ultrasound – Possible Future Treatment

This procedure is currently being researched so it is not routinely available. It uses ultrasound to generate sufficient heat to cause death of tumor cells within a fibroid. The ultrasound is directed to the appropriate position by using real-time magnetic resonance imaging (MRI) to guide the process. The result is death of the fibroid tissue both in and around the treated area.

Thermoablative ultrasound is a noninvasive procedure that appears to cause little pain or other adverse effects. Its effectiveness in alleviating symptoms is currently being studied.

Reference: Stewart EA et al., Focused ultrasound treatment of uterine fibroid tumors: Safety and feasibility of a noninvasive thermoablative technique. *Am J Obstet Gynecol* 2003;189:48-54.

Mifepristone – Possible Future Treatment

Mifepristone, taken by mouth in tablet form, blocks progesterone receptor activity. *This drug has begun to be researched for use with uterine fibroids, but is not approved for fibroids at this time.* A recent small study showed that by the end of 6 months of daily, low-dose treatment, uterine fibroids had shrunk by ~50%. Side effects included amenorrhea and increased growth of the uterine lining. Further evaluation is needed before this treatment can be prescribed routinely by health professionals. **Reference:** Eisinger SH et al. Low-dose mifepristone for uterine leiomyomata. *Obstet Gynecol* 2003;101:243-250.